WHAT IS CLAIMED IS:

1. An isolated and purified nucleic acid molecule comprising a nucleic acid segment encoding a vertebrate DNA repair polypeptide, a biologically active subunit or variant thereof, wherein the polypeptide has a molecular weight of about 95000 Da as determined by SDS-PAGE.

2. The nucleic acid molecule of claim 1 wherein the nucleic acid segment comprises SEQ ID NO:1.

3. The nucleic acid molecule of claim 1 wherein the DNA encodes a polypeptide having SEQ ID NO:2.

4. An isolated and purified DNA molecule comprising SEQ ID NO:1, or a DNA molecule complementary thereto.

5. A method of altering the amount of a DNA repair polypeptide in a cell, comprising:

   (a) introducing into a host cell the isolated nucleic acid molecule of claim 1 operably linked to a promoter functional in the host cell, so as to yield a transformed host cell; and

   (b) expressing the nucleic acid molecule in the transformed host cell as recombinant DNA repair polypeptide, wherein the amount of the recombinant polypeptide produced by the transformed cell is different than the amount of the DNA repair polypeptide produced by a corresponding untransformed cell.

6. A method of altering the amount of a DNA repair polypeptide in a cell, comprising:

   (a) introducing into a host cell a DNA segment comprising the complement of at least a portion of the nucleic acid molecule of claim 1 operably linked to

a promoter functional in the host cell, so as to yield a transformed host cell; and

(b) expressing the DNA segment in the transformed host cell as antisense RNA so as to decrease the amount of the DNA repair polypeptide in the transformed cell.

7. An isolated, purified polypeptide having SEQ ID NO:2, or a biologically active subunit or variant thereof.

8. A fusion polypeptide comprising at least a portion of a DNA repair polypeptide having a molecular weight of about 95000 Da, a biologically active subunit or variant thereof.

9. An isolated, purified antibody that specifically binds to a DNA repair polypeptide having a molecular weight of about 95000 Da as determined by SDS-PAGE, a subunit or variant thereof.

10. A diagnostic method for detecting nucleic acid encoding a DNA repair protein, comprising:

(a) contacting an amount of DNA obtained by reverse transcription of RNA from a mammalian physiological sample which comprises cells, with an amount of at least two oligonucleotides under conditions effective to amplify the DNA encoding a DNA repair protein, or a subunit or variant thereof, by a polymerase chain reaction so as to yield an amount of amplified DNA, wherein the DNA repair protein has a molecular weight of about 95000 Da, as determined by SDS-PAGE, and wherein at least one oligonucleotide is specific for the DNA encoding the DNA repair protein; and

(b) detecting or determining the presence or absence of the amplified DNA.

11. A method for detecting a predisposition for cancer in a mammal, comprising:

a promoter functional in the host cell, so as to yield a transformed host cell; and

(b) expressing the DNA segment in the transformed host cell as antisense RNA so as to decrease the amount of the DNA repair polypeptide in the transformed cell.

7. An isolated, purified polypeptide having SEQ ID NO:2, or a biologically active subunit or variant thereof.

8. A fusion polypeptide comprising at least a portion of a DNA repair polypeptide having a molecular weight of about 95000 Da, a biologically active subunit or variant thereof.

9. An isolated, purified antibody that specifically binds to a DNA repair polypeptide having a molecular weight of about 95000 Da as determined by SDS-PAGE, a subunit or variant thereof.

10. A diagnostic method for detecting nucleic acid encoding a DNA repair protein, comprising:

(a) contacting an amount of DNA obtained by reverse transcription of RNA from a mammalian physiological sample which comprises cells, with an amount of at least two oligonucleotides under conditions effective to amplify the DNA encoding a DNA repair protein, or a subunit or variant thereof, by a polymerase chain reaction so as to yield an amount of amplified DNA, wherein the DNA repair protein has a molecular weight of about 95000 Da, as determined by SDS-PAGE, and wherein at least one oligonucleotide is specific for the DNA encoding the DNA repair protein; and

(b) detecting or determining the presence or absence of the amplified DNA.

11. A method for detecting a predisposition for cancer in a mammal, comprising:

(a) contacting an amount of DNA obtained by reverse transcription of RNA from a mammalian physiological sample which comprises cells, with an amount of at least two oligonucleotides under conditions effective to amplify DNA encoding a DNA repair protein, a subunit or variant thereof, by a polymerase chain reaction so as to yield an amount of amplified DNA, wherein at least one oligonucleotide is specific for the isolated DNA molecule of claim 1; and

(b) detecting or determining the amount of the amplified DNA from the sample in step (a) relative to the amount of amplified DNA in a control sample obtained by reverse transcription of RNA from a mammalian physiological sample which comprises cells having and expressing two copies of a gene encoding the DNA repair protein, wherein a reduced amount of amplified DNA in step(a) is indicative of a predisposition to cancer in said mammal.

12. A method to detect a deletion in a gene encoding a DNA repair protein in a mammalian physiological sample, comprising:

(a) contacting a first amount of a labeled probe comprising at least a portion of the nucleic acid molecule of claim 1 with the sample which comprises mammalian cells, for a sufficient time to form binary complexes between at least a portion of said amount of probe and a portion of the cells in the sample; and

(b) detecting or determining the amount of binary complexes of step (a) relative to the amount of binary complexes formed between a second amount of said probe and a sample comprising mammalian cells which contains and expresses two complete copies of the DNA repair protein gene, wherein a relative lesser amount of binary complexes formed in step (a) is indicative of deletion of at least a portion of the gene.

13. A method to determine genetic modifications of a DNA repair protein gene in a mammalian physiological sample suspected of containing a genetically modified gene, comprising:

(a) subjecting DNA isolated from the sample to a polymerase chain reaction using a plurality of primers under reaction conditions sufficient to amplify at least a portion of said gene to produce an amplification product, wherein the DNA repair protein has a molecular weight of about 95000 Da as determined by SDS-PAGE; and

(b) determining whether the amplification product of step (a) is different than an amplification product obtained by subjecting DNA isolated from a control sample which does not comprise genetic modifications of the gene to a polymerase chain reaction using the plurality of said primers under reaction conditions sufficient to amplify at least a portion of the gene.

14. A method for detecting or determining a DNA repair protein in a sample of human physiological fluid comprising cells, comprising:

(a) contacting an amount of an agent which specifically reacts with the DNA repair protein with the sample to be tested for a sufficient time to allow the formation of binary complexes between at least a portion of said agent and a portion of said protein, wherein the DNA repair protein has a molecular weight of about 95000 Da as determined by SDS-PAGE; and

(b) detecting or determining the presence or amount of the protein complexed with said agent.

15. A method for detecting or determining a DNA repair protein in a mammalian tissue sample, comprising:

(a) mixing an amount of an agent which binds to the DNA repair protein with the cells of the mammalian tissue sample so as to form a binary complex comprising the agent and the cells, wherein the DNA repair protein has a molecular weight of about 95000 Da as determined by SDS-PAGE; and

(b) determining or detecting the presence or amount of complex formation in the sample.

16. A transgenic mouse whose cells contain a chimeric DNA sequence, said chimeric DNA sequence comprising:

a transcription control sequence and the isolated nucleic acid molecule of claim 1, wherein the transcription control sequence and the nucleic acid molecule are operatively linked to each other and are integrated into the genome of the mouse, and wherein the nucleic acid molecule is expressed in the transgenic mouse so as to result in said mouse exhibiting increased amounts of the DNA repair polypeptide.

17. A method of using a transgenic mouse to screen for an agent that modulates a DNA repair polypeptide, comprising:

(a) administering the agent to the transgenic mouse, wherein the transgenic mouse comprises a chimeric DNA sequence comprising a transcription control sequence operatively linked to the nucleic acid molecule of claim 1, wherein the chimeric DNA sequence is integrated into the genome of the mouse, and wherein the nucleic acid molecule is expressed as the DNA repair polypeptide in the transgenic mouse; and

(b) determining whether said agent modulates the amount of the DNA repair polypeptide in the transgenic mouse relative to a transgenic mouse of step (a) which has not been administered the agent.

18. A recombinant mouse, the genome of which does not encode a functional DNA repair protein having a molecular weight of about 95000 Da as determined by SDS-PAGE.

19. An isolated, purified monoclonal antibody that specifically binds Mre11, a biologically active subunit or variant thereof.

20. An isolated, purified antibody or a fragment thereof that specifically binds to a human DNA double strand break repair polypeptide having a molecular weight of 95000 Da as determined by SDS-PAGE wherein the polypeptide comprises SEQ ID NO:2.

2 1
21. The antibody of claim 20 which is a polyclonal antibody.

3 1
22. The antibody of claim 20 which is a monoclonal antibody.

4 1
23. The antibody of claim 20 which binds to amino acids 399-751 of SEQ ID NO:2.

5 1
24. The antibody of claim 20 which binds to a polypeptide consisting of SEQ ID NO:2.

chromosomes and the hybridization signal merged using image analysis software (NU200 and Image 1.57).

Figure 10. Analysis of p95 and the hRad50/hMre11 complex in NBS cells. (A) Crude extracts of normal cells (TK6, 37Lu, IMR90, and K562), an AT cell line (AT3BI), and NBS cells (JS, KW, W1799, DST, GM7078) were subjected to Western blot with p95 antiserum. (B) Immunoprecipitations were carried out on crude extracts from JS cells (NBS) and control cell line TK6 hMre11 antiserum (hMre11 IP) or preimmune serum (PI). The resulting precipitates were subjected to Western blotting analysis with hMre11, hRad50, and p95 antisera. The positions of the three proteins are indicated on the left.

Figure 11. Ionizing Radiation Induced Foci (IRIF) formed by p95 and hMre11 in 37Lu and NBS cells. Irradiated 37Lu primary fibroblasts were harvested at 8 hours post-irradiation, fixed, and probed with p95 antiserum and hMre11 mAb 8F3 (A→D). Images were captured of the same nuclei under FITC (11A, p95), Texas Red (11B, hMre11), DAPI (11C) filters and merged (11D) in Adobe Photoshop. Normal IMR90 fibroblasts (E-N) and W1799 NBS fibroblasts (M-X) were assessed for the ability to form IRIF. Unirradiated (E-H, K-L, O-R, U, V) or irradiated (I-J, M-N, S-T, W-X) cells were harvested at 8 hours post-treatment, fixed, and stained with DAPI and three different antibodies. Panels F, O are p95 preimmune serum; F, L are the corresponding DAPI stains. Panels G, I, Q, S, are stained with p95 antiserum; H, J, R, T are the corresponding DAPI stains. Panels K, M,U, W are stained with hMre11 antiserum; L, N, V, X are the corresponding DAPI stains.

Figure 12. Codons for specified amino acids.

Figure 13. Exemplary and preferred amino acid substitutions.

Figure 14. cDNA sequence of p95 (SEQ ID NO:1).

Figure 15. Amino acid sequence of p95. (SEQ ID NO:2)

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